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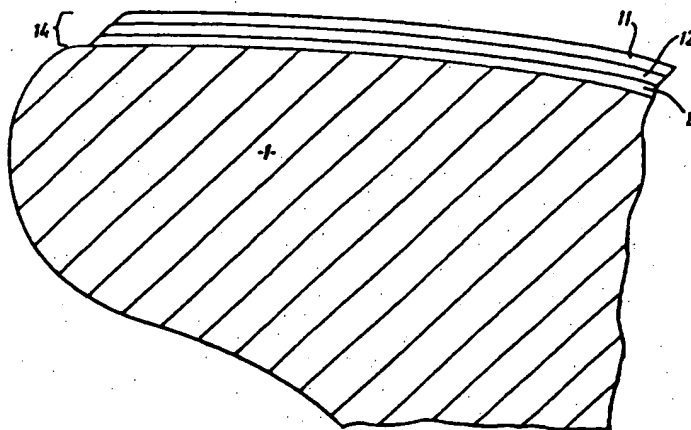
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(54) Title: MEDICAL DEVICE TREATED WITH A HYDROPHILIC POLYMER COMPOSITION



(57) Abstract

There is provided medical devices for use as cardiac, coronary or vascular prostheses, for example heart valves, coronary artery bypass grafts and arterial grafts. The devices described are at least partially coated or impregnated with a hydrophilic polymer composition which desirably contains of from 1 to 99 % by weight of water, preferably 50 to 95 % by weight of water. The hydrophilic polymer composition may be biodegradable and preferably contains a polyurethane. Optionally the hydrophilic polymer composition may contain a pharmaceutically active agent, for example an anti-coagulant, a thrombolytic agent or an antibiotic. The device may be treated with two or more hydrophilic polymer compositions in separate coatings; a triple-layered coating may be especially beneficial. The presence of the hydrophilic polymer coating is beneficial in reducing the thrombogenesis which may occur following implantation of the device

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1 **"Medical Device Treated with a Hydrophilic Polymer**
2 **Composition"**

3
4 The present invention relates to medical implants and
5 equipment having a hydrophilic polymer composition
6 coating. In particular, the present invention is
7 concerned with cardiac implants and vascular
8 prostheses.

9
10 In mammals the heart is a vital organ responsible for
11 maintaining an adequate flow of blood (and hence oxygen
12 and nutrients) to all parts of the body. Essentially
13 the heart acts as a mechanical pump, forcing the blood
14 delivered to it via veins out along arteries at higher
15 pressure. The blood is prevented from flowing
16 backwards through the heart by the presence of valves
17 located therein.

18
19 Dysfunction of one or more of the valves in the heart
20 can have serious medical consequences. Dysfunction of
21 heart valves may be the result of a congenital defect,
22 or of disease-induced damage or degeneration.
23 Dysfunction frequently results from stenosis or
24 narrowing of the valve aperture, preventing sufficient
25 blood through-flow. Further, dysfunction also

1 frequently results from valve insufficiency. In
2 addition to cardiac valve replacement operations,
3 operations for coronary bypass are also frequently
4 required.

5
6 To date, the only solution to treat severe heart valve
7 dysfunction is to replace the malfunctioning valve.
8 Such a valve replacement operation, in addition to
9 being extremely costly, requires complex open-heart
10 surgery. There is also a finite number of times that
11 a heart valve can be replaced successfully for any
12 particular patient, making the design and operational
13 lifetime of any replacement valve extremely important.

14
15 Mechanical valves have been developed and used for
16 heart valve replacement operations. Whilst such valves
17 exhibit excellent operational lifetimes, they suffer
18 from a higher incidence of thrombosis (blood clotting)
19 due to the trigger of clotting in the blood as the
20 material of the valve is recognised by the immune
21 system as being "foreign" to the body. Suitable heart
22 valves are manufactured, for example, by Aortech Europe
23 Limited, Strathclyde, UK under the name ULTRACOR (Trade
24 Mark). Heart valves manufactured by St Jude Medical,
25 CarboMedics, Medtronic or ATS Medical, USA are all
26 suitable as are valves manufactured by Sorin, Italy

27
28 Currently mechanical valve implants are estimated at
29 110,000 implants worldwide with an average price of
30 between US\$2,000 and \$3,000 retail to the hospital.
31 The one major clinical problem facing mechanical valves
32 is anti-coagulation. It is currently believed that the
33 majority of emboli and clots initially grow from the
34 junction of the sewing ring with the metal or pyrolite
35 housing. Also suture material and large knots put in

1 place when the surgeon implants the valve may be the
2 cause of some of these phenomena. Currently no
3 manufacturer has an anti-thrombogenic coating on their
4 valves and the ability to do this with the consequent
5 lowering of the frequency of embolic episodes or the
6 more catastrophic thrombosis which can lead to death of
7 the patient would be highly desirable.

8
9 In an effort to reduce the risk of thrombosis to a
10 patient, it has been proposed (see for example EP-A-
11 0,402,036 of ProMedica International Inc) to use
12 porcine pulmonary valves in human patients.
13 Surprisingly such xenografts show less tendency to be
14 destroyed by the recipient, especially where the donor
15 organ has been pre-treated with glutaraldehyde to
16 reduce the risk of calcification. However, such valves
17 have a finite lifetime and must generally be replaced
18 within 10 years of implantation.

19
20 With increasing life expectancy for humans, there is a
21 corresponding rise in patients requiring cardiac valve
22 replacement and/or coronary bypass operations. There
23 is thus an increasing need for cardiac and vascular
24 prostheses having both an extended useful lifetime and
25 also a low risk of inducing thrombosis in a recipient.

26
27 It has now been found that coating or impregnating at
28 least part of a cardiac prosthesis (such as a heart
29 valve) with a hydrophilic polymer composition
30 significantly reduces thrombogenesis.

31
32 The present invention thus provides a cardiac, coronary
33 or vascular prosthesis having a coating of hydrophilic
34 polymer composition on at least a part thereof and/or
35 being at least partially impregnated with a hydrophilic
36 polymer composition.

1 Viewed from a further aspect the present invention
2 provides a heart valve wherein at least part of the
3 valve (for example the sewing ring and/or the junction
4 of the sewing ring with the heart valve housing) is
5 coated or impregnated with a hydrophilic polymer
6 composition.

7
8 Viewed from a yet further aspect the present invention
9 provides a prosthesis (for example coronary artery
10 bypass grafts and arterial grafts) suitable for
11 coronary bypass operations and vascular surgery wherein
12 at least part of the surface to be contacted by bodily
13 fluids (preferably substantially all of such surfaces)
14 is coated or impregnated with a hydrophilic polymer
15 composition.

16
17 In coronary bypass operations surgeons currently
18 harvest the saphenous vein from the patient's leg,
19 which often causes the patient post-operatively more
20 pain problems than the thoracotomy. It is estimated
21 that after ten years a significant number of all
22 coronary artery bypass grafts are either grossly
23 inefficient at providing extra blood flow to the
24 ischemic part of the heart or have completely clotted
25 and closed down. An artificial coronary artery bypass
26 graft, which would be coated or impregnated completely
27 with an anti-thrombogenic material would be desirable
28 despite the fact that vein grafts are harvested free.

29
30 Where the prosthesis is a mechanical heart valve, the
31 hydrophilic polymer composition may be present on the
32 sewing ring thereof and/or on the junction of the
33 sewing ring with the metallic part of the valve
34 housing, Suitable sewing ring material which may be
35 coated according to the present invention includes
36 T flon.

1 Optionally, the hydrophilic polymer composition may
2 coat or be used to impregnate substantially all of the
3 surfaces of the coronary prostheses or vascular grafts.

4
5 The hydrophilic polymer composition may contain of from
6 1% to 99% water (by weight), for example said
7 composition may contain 20% to 99% water, especially 40
8 to 95% water. The composition will normally be liquid
9 at ambient temperature and may be sprayed or painted
10 onto the device of the present invention.
11 Alternatively the device may be dipped into the
12 composition and allowed to dry thereon.

13
14 Desirably, the hydrophilic polymer has low surface
15 adhesion properties, thus reducing the incidence or
16 risk of thrombogenesis.

17
18 Suitable hydrophilic polymers are described in US-A-
19 4,256,066; US-A-4,156,067; US-A-4,255,550;; US-A-
20 4,359,588; US-A-4,408,023; US-A-4,424,305; US-A-
21 4,490,432; US-A-4,496,535; US-A-4,729,914; US-A-4,743,
22 673; US-A-4,780,512; US-A-4,789,720; US-A-4,798,876;
23 US-A-4,810,582; US-A-5,000,955 and US-A-4,789,720
24 all of Tyndale Plains Hunter Ltd, Princeton, New
25 Jersey.

26
27 In particular, the hydrophilic polymers may be
28 polyurethanes, as described in US-A-5,120,816 and in
29 US-A-4,789,720. The polymers exemplified in US-A-
30 4,789,720 and in US-A-5,120,816 are especially
31 suitable.

32
33 The advantageous biomedical properties of certain
34 hydrophilic polymers suitable for use in the present
35 invention (for example as disclosed in US-A-4,789,720
36 and in US-A-5,120,816) derive from the structure of the

1 polymers which are prepared by reacting an aliphatic
2 diisocyanate with different polyoxyalkylene glycols,
3 usually with a majority of polyoxyethylene glycol. The
4 polymers contain terminal hydroxyl groups and can be
5 made to different molecular weights and degrees of
6 hydrophilicity by adjusting the ratio of hydrophilic to
7 hydrophobic glycol. The hydrophilicity of these
8 polymers can be varied over a wide range, from
9 extremely hydrophilic to hydrophobic polymers as
10 required. Preferably, the polymer composition contains
11 of from 50 to 95% water. The polymer will normally
12 have an average molecular weight range of about 10,000
13 to 200,000.

14
15 In one embodiment, the hydrophilic polymers are
16 biodegradable. Mention may be made of the polyurethane
17 polymers of US-A-4,789,720 and of US-A-5,120,816 which
18 are degraded over time to produce urea, which is then
19 excreted from the body in urine. The time taken for
20 the polymer to be degraded and thus the operational
21 lifetime of the polymer composition may be varied by
22 adjusting or modifying the chemical nature of the
23 polymer structure. Such modification can be carried
24 out during manufacture of the polymer, or may be a
25 post-production modification to the polymer.

26
27 Alternatively, a polymer which is viewed as non-
28 biodegradable within the art may be used and this may
29 be preferred in certain aspects.

30
31 In a further embodiment, the hydrophilic polymer
32 composition may be used as a carrier for
33 pharmaceutically active agents. Suitable agents
34 include immuno-suppressant drugs (to reduce the risk of
35 prosthesis rejection or to combat such rejection
36 reaction); anti-bacterial agents, such as antibiotics

1 (to reduce the risk of infection or to combat infection
2 introduced during the operation to implant the
3 prosthesis), growth factor regulators and anti-
4 coagulant, anti-thrombogenic or thrombolytic drugs (to
5 reduce the risk or to combat thrombosis and emboli
6 formation). Mention may be made of heparin, heparin
7 fragments tissue-type plasminogen activator (tPA),
8 urokinase (uPA), anti-thrombosis agents (such as
9 Hirudan) and albumin, as examples of suitable anti-
10 coagulant agents to combat thrombosis. Also suitable
11 are anti-coagulant agents which are antibodies (for
12 example antibodies directed against platelet receptor
13 GPIb and/or GPIIb/IIIa, against platelet receptor GPIIb/IIIa,
14 and/or against von Willebrand Factor (vWF)) and also
15 such agents with vasoactive properties (such as
16 Prostacyclin and Nitric Oxide). With regard to
17 pharmaceutically active agents which act as growth
18 factor regulators particular mention may be made of
19 antibodies, such as antibodies directed against
20 Platelet-derived Growth Factor (PDGF), Fibroblastic
21 Growth Factor (FGF), Transforming Growth Factor beta
22 (TGF), Insulin-like Growth Factor (IGF), Interleukins
23 (IL1-8), Endothelin, Thrombin, and/or Endothelial
24 adhesion molecules eg ICAM-1. Also suitable are
25 angiotensin converting enzyme (ACE) inhibitors (for
26 example Captopril), and endothelial cell growth factor
27 (ECGF). In certain aspects use of anti-sense
28 oligonucleotides or antibodies to particular mRNAs may
29 be advantageous, for example anti-sense
30 oligonucleotides to a -myc, PCNA and the like or
31 antibodies to the mRNA molecules encoding for growth
32 factors.

33

34 Suitable antibiotics which may advantageously be
35 present in the polymer of the invention include
36 Penicillins, Cephaolsporins, Aminoglycosides,

1 Tetracyclines, Macrolides, Glycopeptides eg Vancomycin,
2 Teicoplanin, Sulphonamides and/or Anti-fungals eg
3 Fluconazole. More than one pharmaceutically active
4 agent may be present.

5
6 The pharmaceutically active agent may be chemically
7 bound (for example via a covalent or ionic bond) to the
8 hydrophilic polymer. Alternatively, the
9 pharmaceutically active agent may be physically
10 entrapped within the polymer and released as the
11 polymer degrades in the body.

12
13 In certain instances it may be desirable to have more
14 than one coating on said prostheses. Thus, for example
15 the hydrophilic polymer (optionally comprising a
16 pharmaceutically active agent) may itself be coated,
17 for example with a delay release coating or more
18 preferably may itself be coated with a further coating
19 of hydrophilic polymer.

20
21 In an analogous manner, there may be three or more
22 different layers of hydrophilic polymer coatings. Each
23 layer may be of the same or different chemical
24 composition (ie chemical structure of the hydrophilic
25 polymer and/or water content thereof) and may contain
26 the same or different amounts of identical or distinct
27 pharmaceutically active agent(s). By careful selection
28 of the layers used to coat a prosthesis, the lifetime
29 of the polymer coatings and/or release of any
30 pharmaceutically active agent comprised therein may be
31 controlled.

32
33 For example a triple-layer coating may be desirable.
34 The first coating immediate to the prosthesis may
35 optionally comprise an agent which is released only
36 slowly, the first coating layer being degradable very

1 slowly over time. Instead of a first coating layer,
2 the prosthesis may be impregnated with such a
3 hydrophilic polymer composition. An intermediate
4 coating may then be coated over said first layer, the
5 intermediate layer having a lifetime of approximately 6
6 weeks and an appropriate amount of pharmaceutically
7 active agent. The top layer covering said intermediate
8 layer may be designed to release an amount of anti-
9 thrombogenic agent over the danger period (extending
10 for approximately 10 days) for producing blood clots
11 and emboli; this being the lifetime of the top layer
12 once in the body.

13
14 Viewed from a further aspect, the present invention
15 provides a method of treating prostheses to reduce the
16 risk (and incidence) of thrombogenesis after
17 implantation in a patient, said method comprising
18 treating at least a part of said prostheses with a
19 hydrophilic polymer composition. Generally, said
20 prostheses may be impregnated and/or coated with said
21 polymer by any suitable conventional means. Mention
22 may be made of producing a polymer film which is then
23 adhered to the prostheses or, more usually, forming
24 said polymer on said prostheses in situ.

25
26 Viewed from a yet further aspect the present invention
27 provides a method of treating cardiac and vascular
28 dysfunction in a patient, said method comprising
29 implanting coronary prostheses coated and/or
30 impregnated with a hydrophilic polymer composition as
31 hereinbefore described.

32
33 In a yet further aspect the present invention provides
34 the use of prostheses coated and/or impregnated with a
35 hydrophilic polymer composition (especially a
36 mechanical heart valve, coronary artery bypass grafts

1 and arterial grafts) for implantation in a patient to
2 relieve cardiac and vascular dysfunction.

3

4 In a still yet further aspect the present invention
5 provides the use of a hydrophilic polymer composition
6 as hereinbefore described to coat and/or impregnate
7 cardiac, coronary or vascular prostheses.

8

9 Viewed from another aspect the present invention
10 provides the use of a hydrophilic polymer composition
11 as hereinbefore described in the manufacture of
12 cardiac, coronary or vascular prostheses for
13 implantation in a patient to relieve coronary or
14 vascular dysfunction.

15

16 Figure 1 is a schematic view in partial cross-section
17 of a conventional heart valve prosthesis.

18

19 Figure 2 is a detailed cross-section of the junction
20 between the sewing ring and heart valve housing of the
21 heart valve prosthesis shown in Figure 1 following
22 implantation into a patient.

23

24 Figures 3 and 4 are schematic partial cross-sections of
25 the conventional heart valve prosthesis of Figure 1 at
26 different stages after implantation in the patient.

27

28 Figure 5 is a cross-section giving details of the
29 attachment of a conventional heart valve to patient
30 tissue.

31

32 Figures 6 and 7 are cross-sections of the heart valve
33 illustrated in Figure 5 following different periods of
34 implantation in the patient.

35

36 Figure 8 is a cross-section of a portion of the sewing

1 ring of the heart valve following treatment with a
2 hydrophilic polymer composition.

3
4 In more detail, Figures 1 to 7 illustrate conventional
5 heart valves as currently used in heart valve
6 replacement surgery. The heart valves illustrated are
7 mechanical prostheses, likely to initiate blood clot
8 formation as shown in Figures 2, 3, 4, 6 and 7.
9 Conventional mechanical heart valve 10 comprise sewing
10 ring 1 which completely surrounds the outer ring of the
11 valve housing 2. There is a junction 3 between the
12 sewing ring 1 and valve housing 2.

13
14 As is illustrated in Figure 5 sewing ring 1 is used to
15 attach the mechanical heart valve 10 into the patient
16 by means of sutures, staples or the like. As
17 illustrated, a suture 6 has been used to extend through
18 sewing ring 1 and a flap of patient tissue 5. The
19 suture 6 is securely fastened with knot 7. Alternative
20 means of attachment of the heart valve 10 into the
21 patient may also be used.

22
23 Following implantation of mechanical heart valve 10
24 into a patient, the heart valve 10 is exposed to the
25 patient's immune system and its near presence within
26 the patient may initiate blood clotting as a form of
27 immune reaction. Blood clotting may be initiated in
28 two locations, in particular the junction 3 between
29 sewing ring 1 and valve housing 2 and also surrounding
30 the suture knot 7. Figure 2 illustrates an initial
31 blood clot 4 which has become established at junction 3
32 between sewing ring 1 and housing 2. The growth of
33 this blood clot is illustrated in Figures 3 and 4.
34 From Figure 4 the blood clot is shown extending
35 vertically down housing 2 and any further increase in
36 size in clot 4 could seriously impair the function of

1 the replacement valve 10.

2

3 Figure 6 illustrates blood clot 4 initially formed at
4 junction 3 between sewing ring 1 and valve housing 2.
5 Additionally a further clot 8 is shown surrounding knot
6 7 of suture 6. Figure 7 illustrates the growth of
7 blood clots 4, 8 following a further period of time,
8 and as illustrated the clots 4, 8 have merged into a
9 single merged blood clot 9 which extends over housing
10 2, junction 3 and a large portion of sewing ring 1,
11 including knot 7. The risk that a portion of clot 9
12 will become detached, thus creating thrombosis or
13 emboli problems within the patient, is high.

14

15 Figure 8 illustrates a portion of sewing ring 1 of a
16 conventional heart valve 10 in cross-section and
17 treated with a layer 14 of a hydrophilic polymer
18 composition. As illustrated only a portion of sewing
19 ring 1 has been treated with the hydrophilic polymer
20 composition, and coating 14 extends across the surface
21 of sewing ring 1 which is particularly vulnerable to
22 initiating blood clot formation. In coating 14 the
23 hydrophilic polymer composition is in fact a composite
24 of three separate layers, each containing a different
25 hydrophilic polymer. Layer 11 which is immediately
26 exposed to the patient's immune system is selected to
27 biodegrade over a three day period and comprises an
28 anti-thrombogenic agent and/or an antibiotic which is
29 controllably released over that timescale to combat
30 blood clot and emboli formation. Intermediate layer 12
31 is designed to biodegrade within a two week period and
32 contains a lesser amount of a pharmaceutically active
33 agent, for example an anti-thrombogenic agent. Layer
34 13 is designed to biodegrade over a six month time
35 scale. The triple-layer coating illustrated in Figure
36 8 is a preferred embodiment of the invention since this

1 arrangement permits a high degree of control
2 immediately following implantation, whilst avoiding
3 unnecessary release of the anti-thrombogenic agent over
4 a much longer timescale, for example over six months.
5 Once coating 14 has completely biodegraded, the
6 patient's immune system will have adapted to the
7 presence of the heart valve 10 and the likelihood of
8 thrombogenesis or emboli formation at that stage is
9 much reduced. Instead of a coating 14, it is also
10 possible for the heart valve 10 to be partially
11 impregnated with a hydrophilic polymer composite.
12
13 It is also possible for a single or dual layer
14 hydrophilic polymer composition to be used, rather than
15 the triple-layer coating illustrated in Figure 8.
16
17 Likewise other mechanical prostheses for cardiac,
18 coronary or vascular surgery may be impregnated or
19 coated with suitable hydrophilic polymer
20 composition(s).

1 CLAIMS

- 2
- 3 1. A cardiac, coronary or vascular prosthesis having
- 4 a coating of hydrophilic polymer or at a part
- 5 thereof and/or being at least partially
- 6 impregnated with a hydrophilic polymer
- 7 composition.
- 8
- 9 2. A prosthesis as claimed in Claim 1 wherein at
- 10 least a part of the surface to be contacted by
- 11 body fluids is coated or impregnated with said
- 12 hydrophilic polymer composition.
- 13
- 14 3. A prosthesis as claimed in Claim 2 wherein
- 15 substantially all of the surface to be contacted
- 16 by body fluids is coated or impregnated with said
- 17 hydrophilic polymer composition.
- 18
- 19 4. A prosthesis as claimed in any one of Claims 1 to
- 20 3 which is a heart valve.
- 21
- 22 5. A prosthesis as claimed in Claim 4 wherein the
- 23 sewing ring and/or the junction between the sewing
- 24 ring and heart valve housing is coated or
- 25 impregnated with said hydrophilic polymer
- 26 composition.
- 27
- 28 6. A prosthesis as claimed in any one of Claims 1 to
- 29 3 which is suitable for coronary bypass operations
- 30 or vascular surgery.
- 31
- 32 7. A prosthesis as claimed in Claim 6 capable of use
- 33 as a coronary artery bypass graft or an arterial
- 34 graft.
- 35
- 36 8. A prosthesis as claimed in any one of Claims 1 to

- 1 7 wherein said hydrophilic polymer composition
2 contains of from 1% to 99% by weight of water.
3
- 4 9. A prosthesis as claimed in Claim 8 wherein said
5 hydrophilic composition contains of from 40 to 95%
6 by weight of water.
7
- 8 10. A prosthesis as claimed in any one of Claims 1 to
9 9 wherein said hydrophilic polymer composition
10 comprises a polyurethane.
11
- 12 11. A prosthesis as claimed in any one of Claims 1 to
13 10 wherein said hydrophilic polymer composition is
14 biodegradable.
15
- 16 12. A prosthesis as claimed in any one of Claims 1 to
17 11 wherein said hydrophilic polymer composition
18 also contains a pharmaceutically active agent.
19
- 20 13. A prosthesis as claimed in Claim 12 wherein said
21 agent has an anti-coagulant, anti-thrombogenic or
22 a thrombolytic activity.
23
- 24 14. A prosthesis as claimed in any one of Claims 1 to
25 13 impregnated or coated with two or more
26 hydrophilic polymer compositions which may be the
27 same or different.
28
- 29 15. A prosthesis as claimed in Claim 14 having a
30 triple-layer coating.
31
- 32 16. A method of treating a cardiac, coronary or
33 vascular prosthesis to reduce thrombogenesis
34 following implantation in a patient, said method
35 comprising treating said prosthesis with a
36 hydrophilic polymer composition.

- 1 17. A method as claimed in Claim 16 wherein said
2 hydrophilic polymer composition is as defined in
3 any one of Claims 8 to 13.
4
- 5 18. The use of a hydrophilic polymer composition as
6 claimed in any one of Claims 8 to 13 to coat or
7 impregnate at least a portion of a cardiac,
8 coronary or vascular prosthesis.
9
- 10 19. The use of a hydrophilic polymer composition as
11 claimed in any one of Claims 8 to 13 manufacture a
12 cardiac, coronary or vascular prosthesis for
13 implantation in a patient to relieve coronary or
14 vascular dysfunction.
15
- 16 20. Use as claimed in either one of Claims 18 and 19
17 wherein said prosthesis is a heart valve.
18

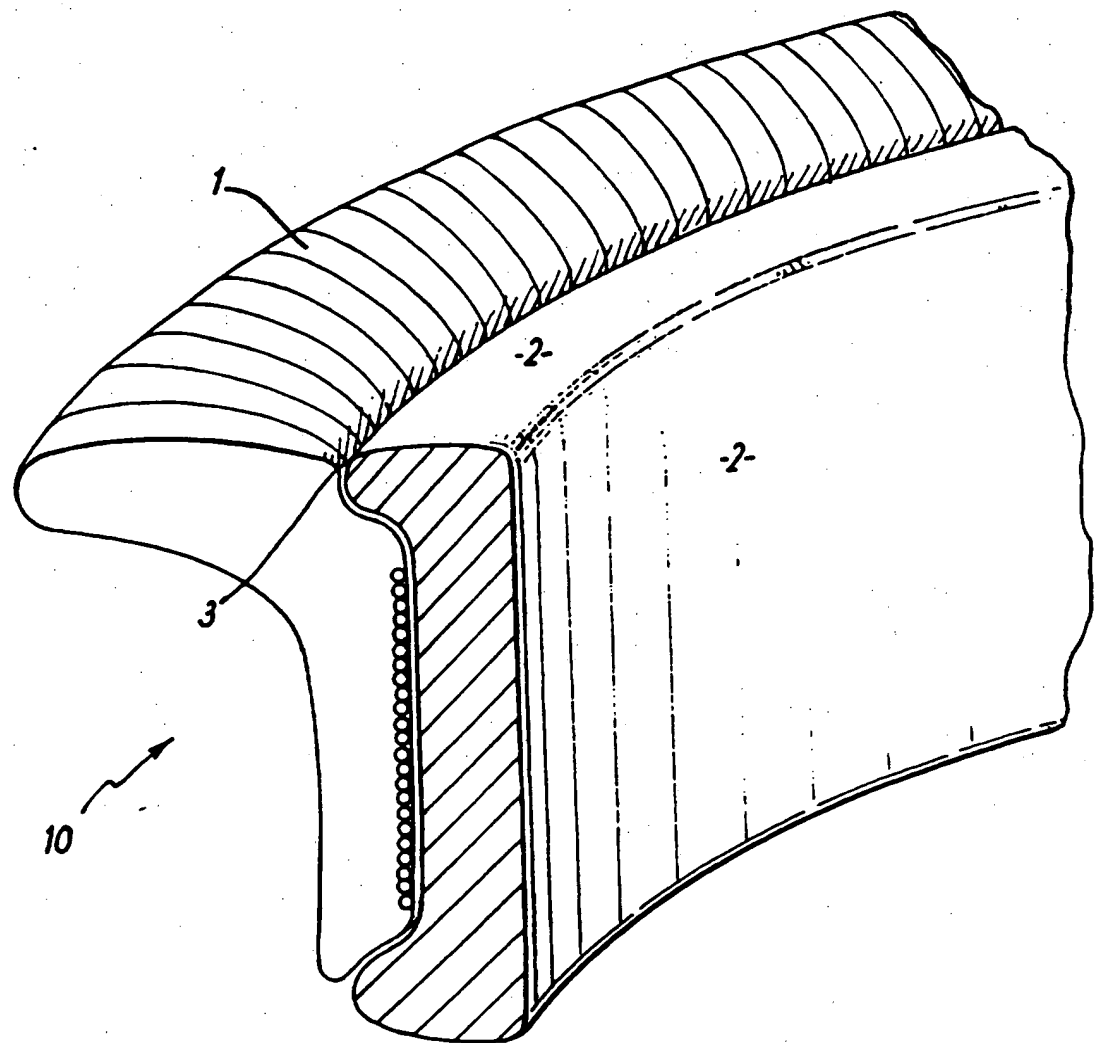


FIG. 1

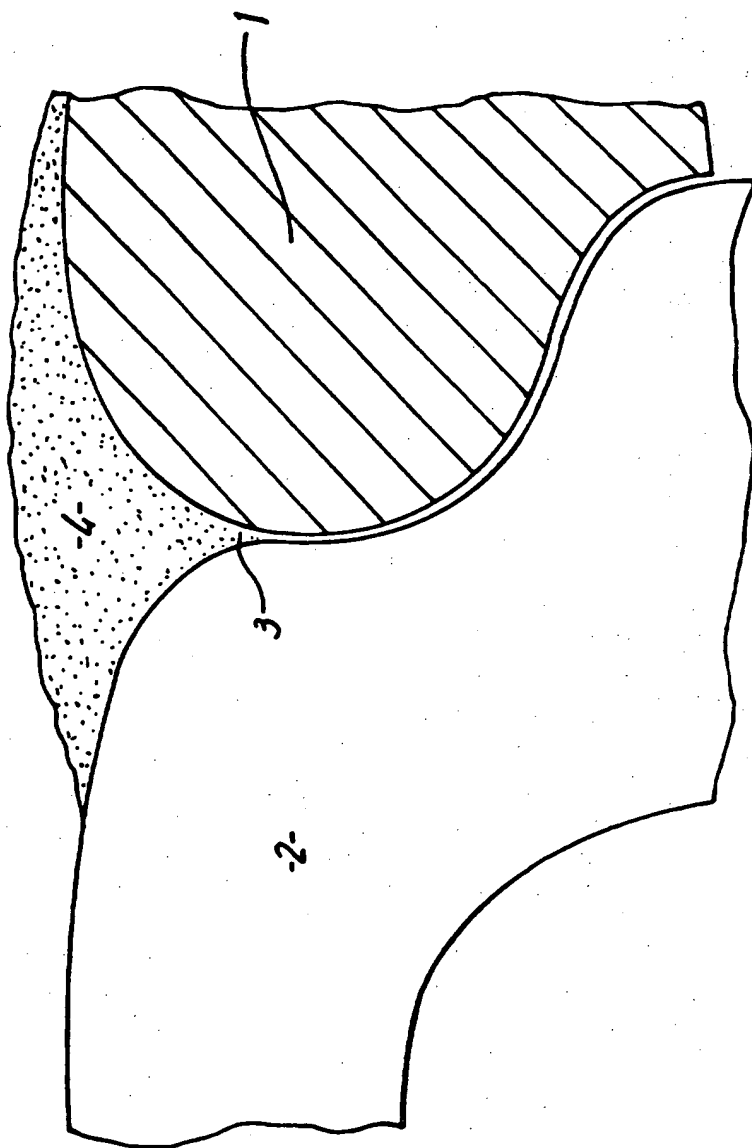


FIG 2

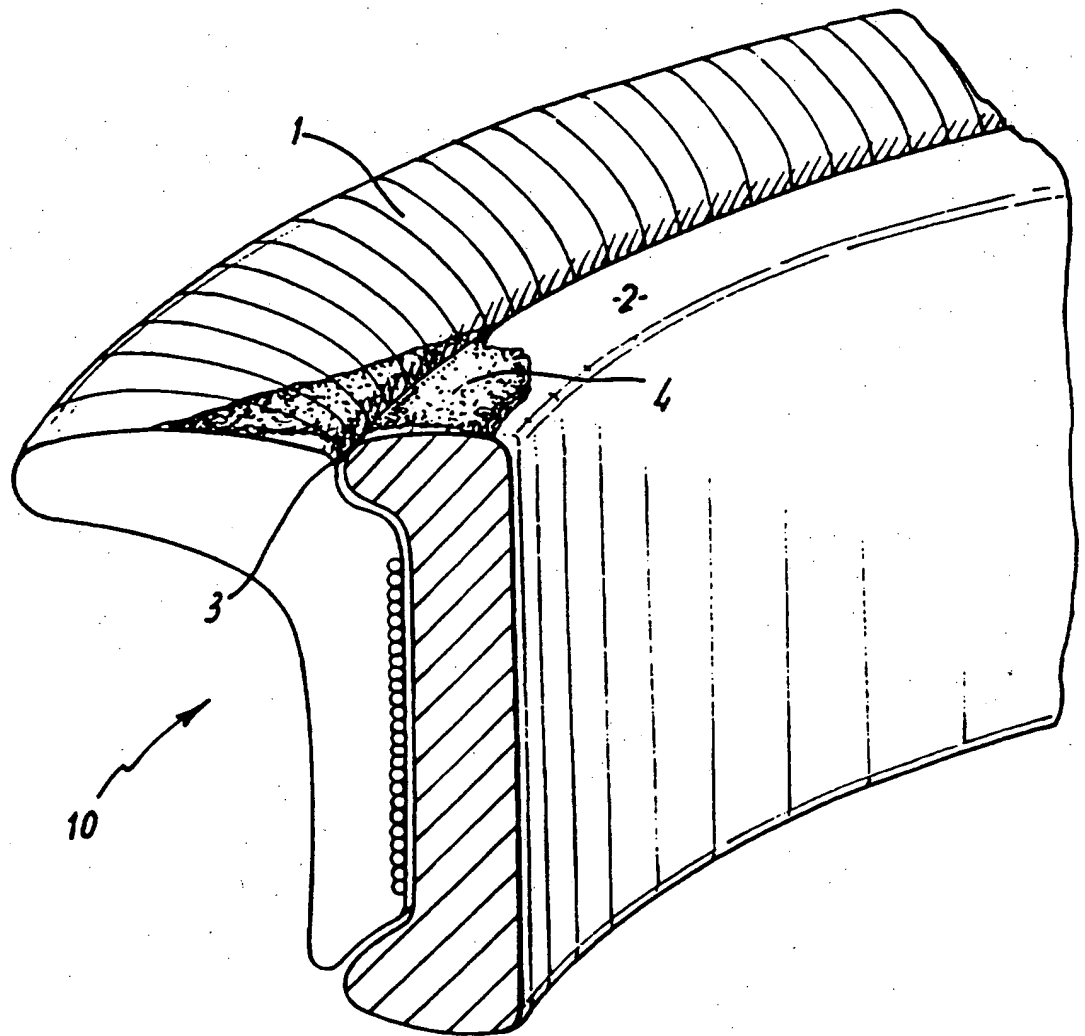


FIG. 3

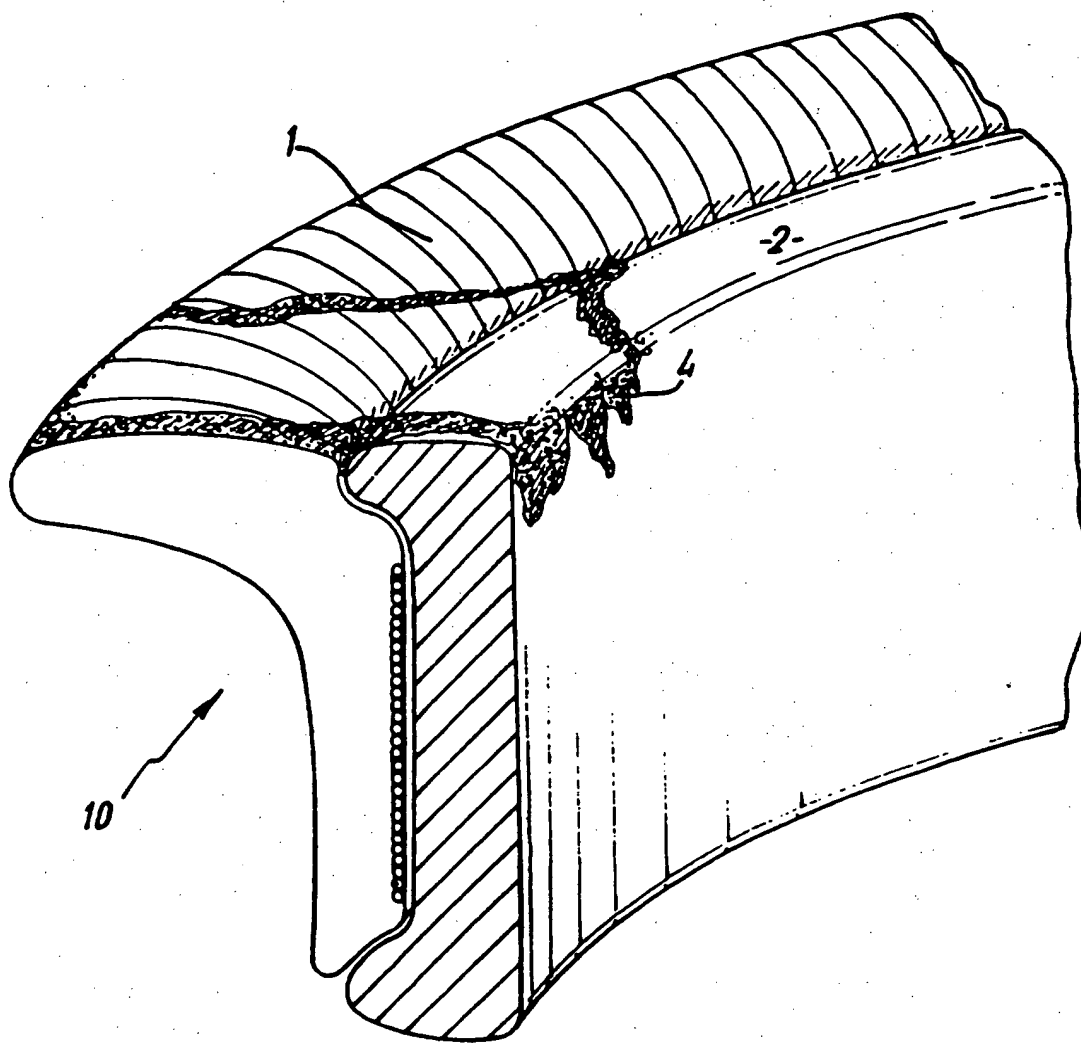


FIG. 4

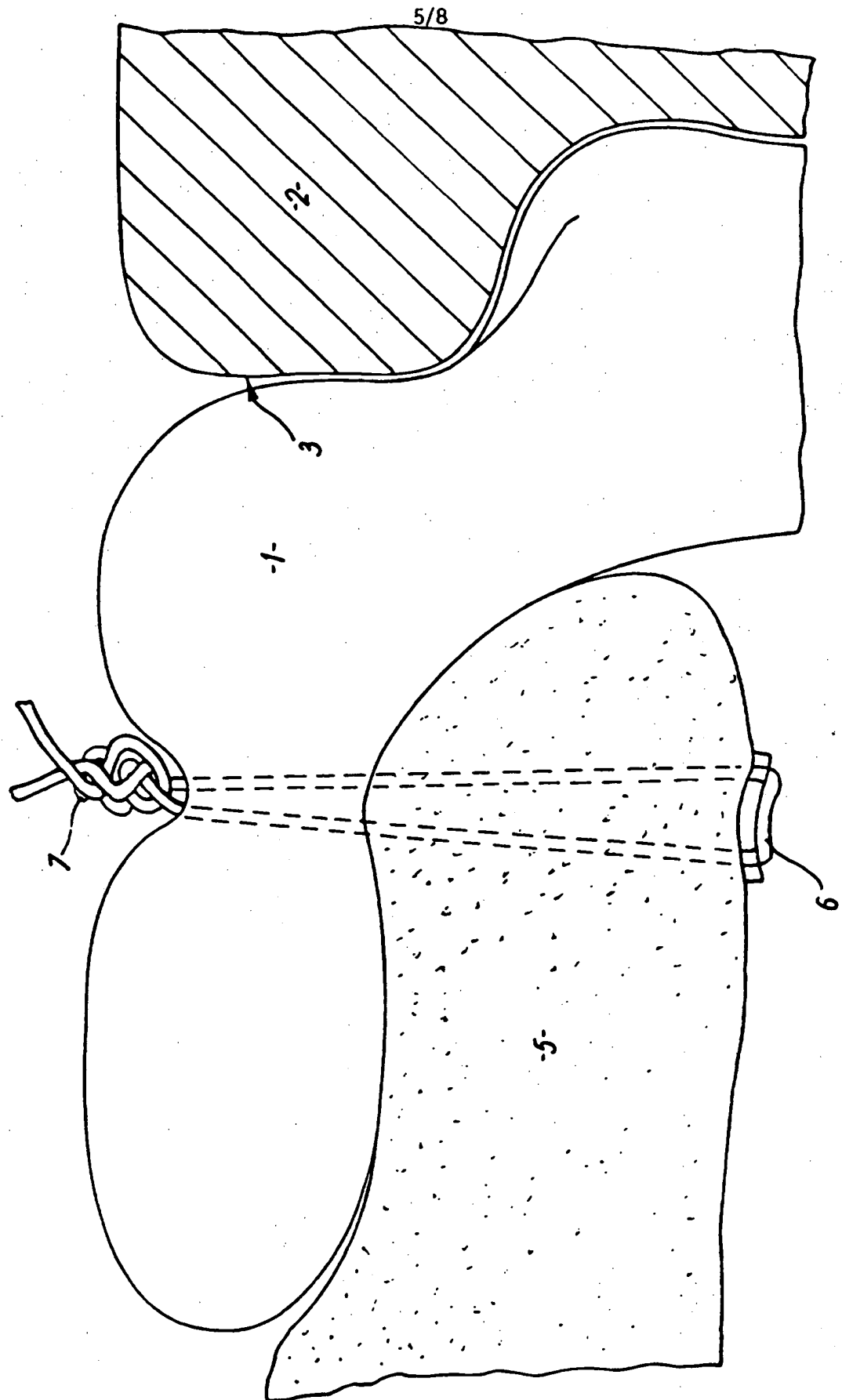


FIG. 5

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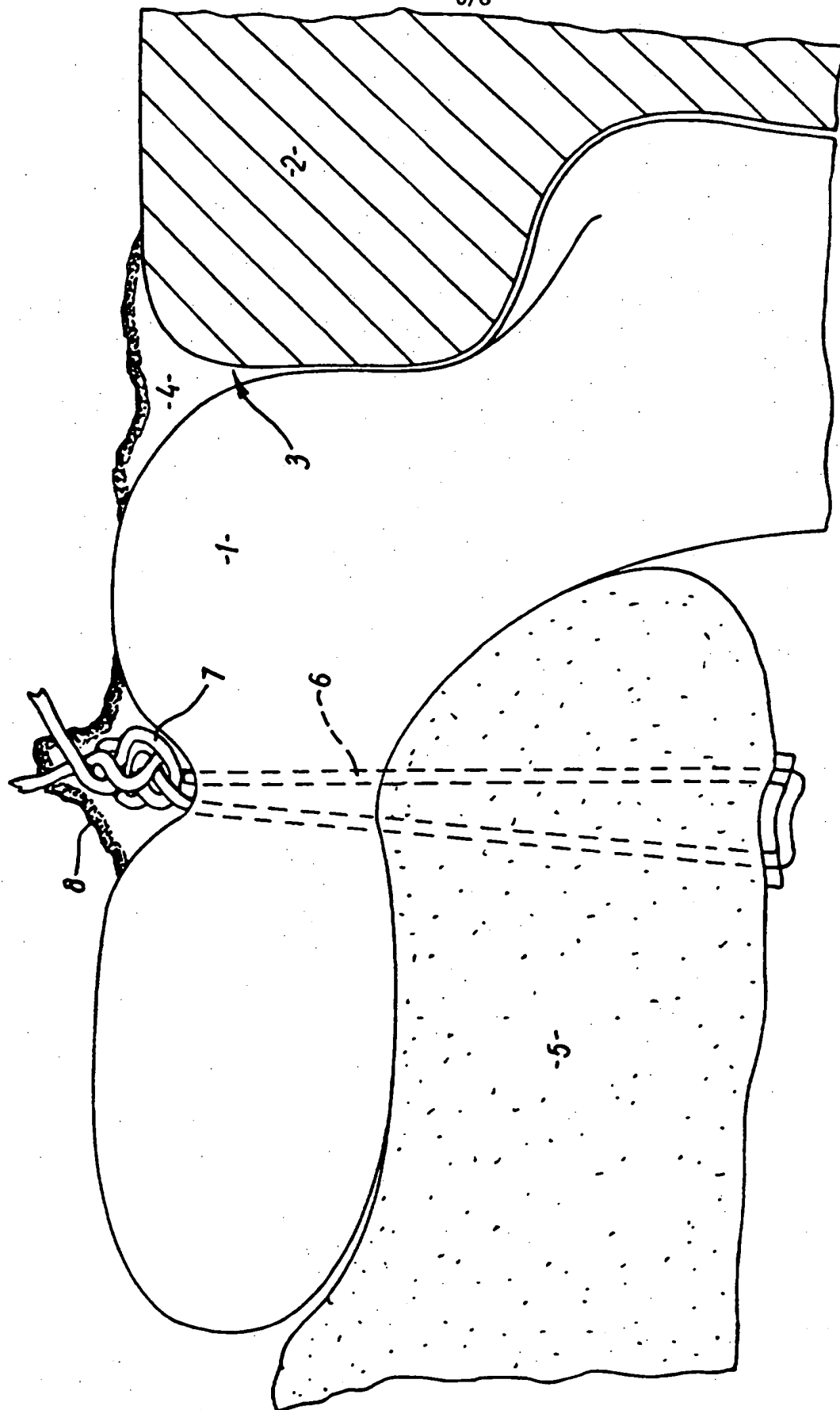


Fig. 6

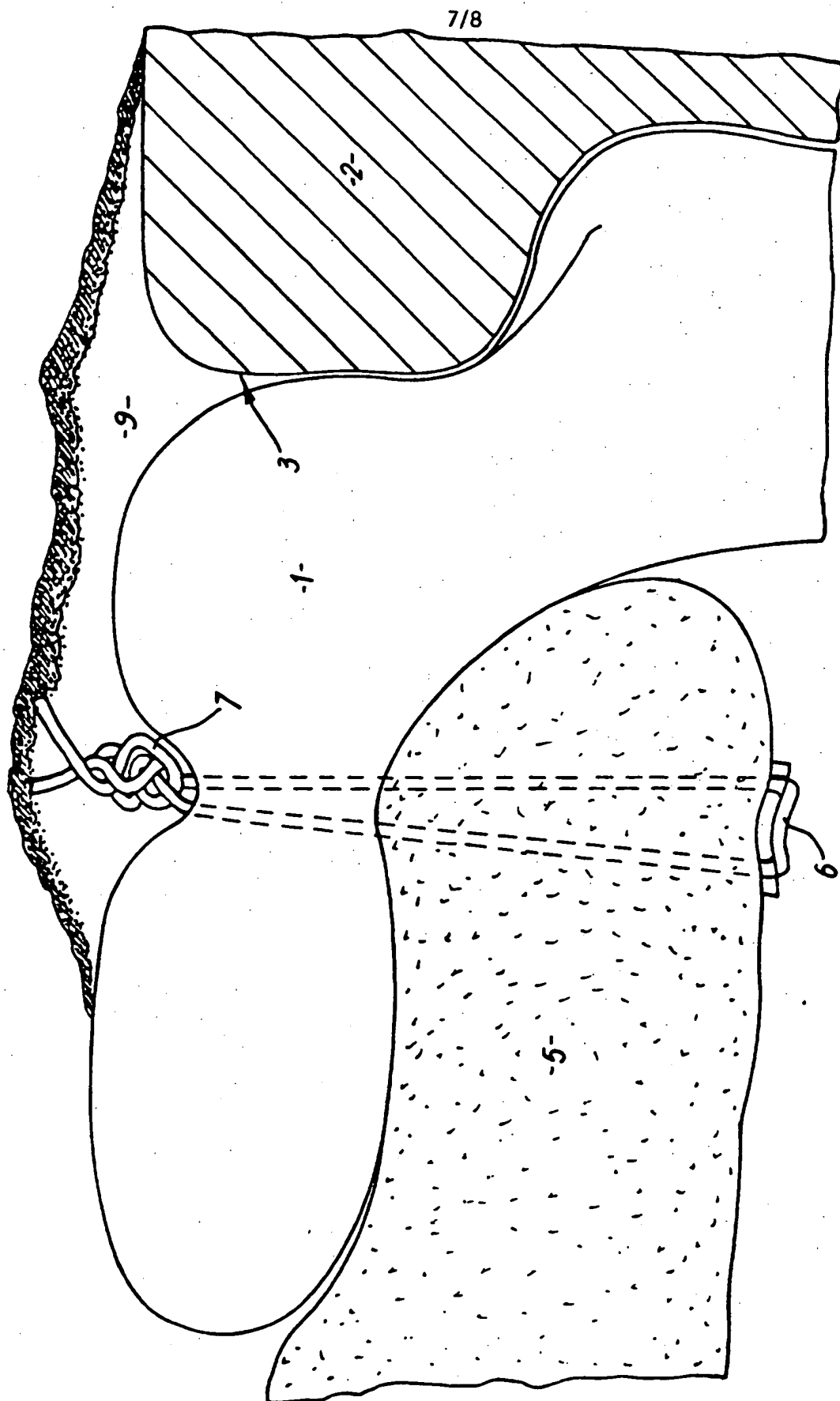


FIG. 7

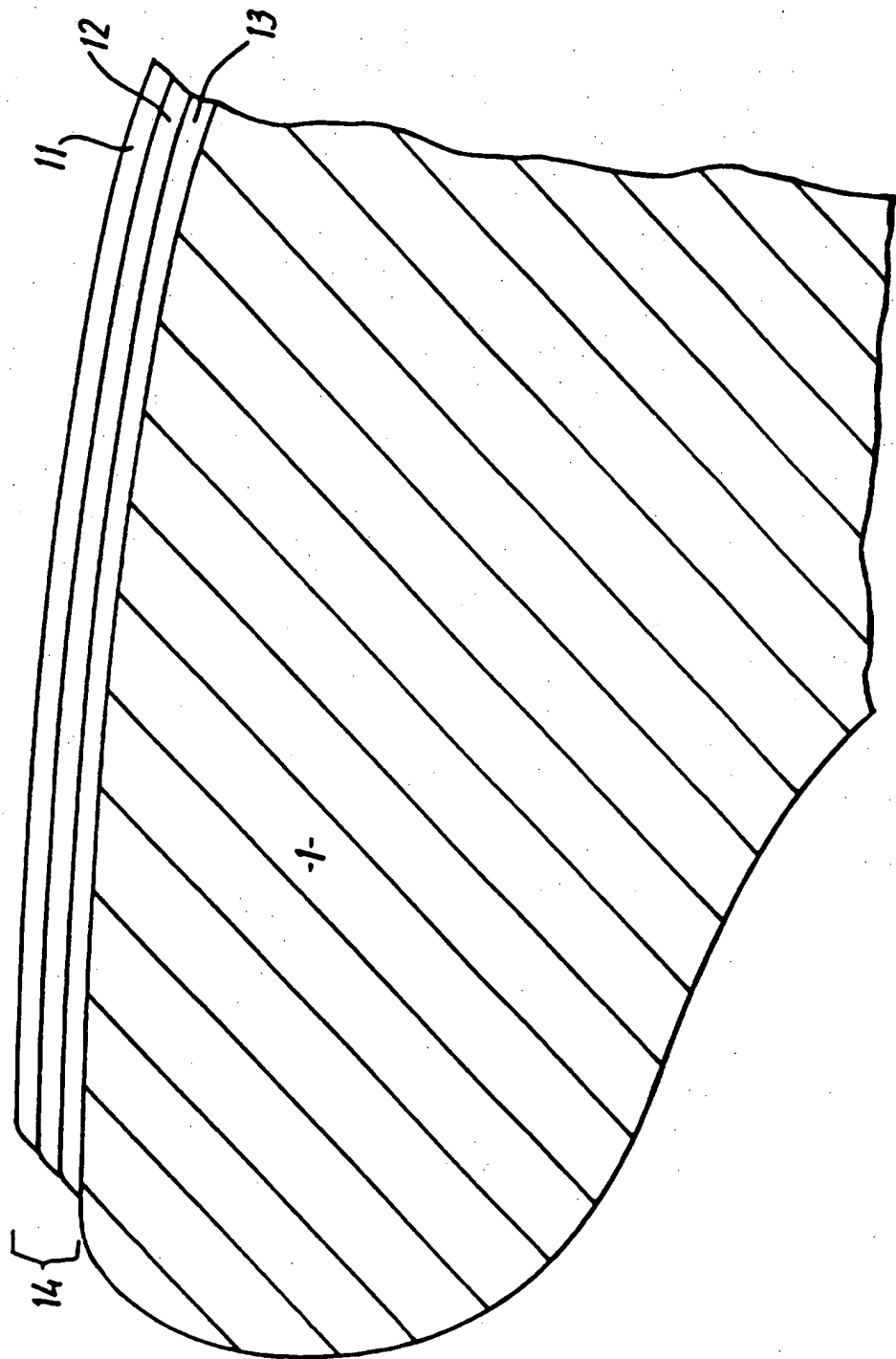


Fig. 8

INTERNATIONAL SEARCH REPORT

International Application No

PC 1/GB 96/00725

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61L27/00 A61L33/00 A61F2/24

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 A61L A61F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO,A,94 21308 (CEDARS SINAI MEDICAL CENTER) 29 September 1994 see page 6, line 15 - line 20; examples 1-4 ---	1-20
X	GB,A,2 255 394 (GALRAM TECHNOLOGY IND LTD) 4 November 1992 see claims ---	1-3
X	EP,A,0 106 004 (INT SILICONE CORP) 25 April 1984 see the whole document ---	1-3
Y	WO,A,90 14054 (IMPRA INC) 29 November 1990 see claims --- -/--	1-20

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

A document member of the same patent family

Date of the actual completion of the international search

1 August 1996

Date of mailing of the international search report

14.08.96

Name and mailing address of the ISA

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Fax (+31-70) 340-3016

Authorized officer

ESPINOSA, M

INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 96/00725

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US,A,4 729 914 (KLIMENT CHARLES K ET AL) 8 March 1988 cited in the application see examples 1-9 ----	1-20
A	EP,A,0 335 308 (GRACE W R & CO) 4 October 1989 see claims ----	1-20
A	WO,A,89 11500 (COMMW SCIENT IND RES ORG) 30 November 1989 see claims ----	1-3
A	US,A,4 119 094 (MICKLUS MICHAEL J ET AL) 10 October 1978 see claims; examples 1,2 ----	1
A	EP,A,0 443 993 (SORIN BIOMEDICA SPA) 28 August 1991 see column 3, line 20 - line 28; claims -----	1-3

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/GB96/00725

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 16, 17
because they relate to subject matter not required to be searched by this Authority, namely:
Remark: Although claims 16 and 17 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 96/00725

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO-A-9421308	29-09-94	EP-A- 0689465	03-01-96
GB-A-2255394	04-11-92	DE-A- 4214098	05-11-92
		FR-A- 2675992	06-11-92
EP-A-0106004	25-04-84	US-A- 4373009	08-02-83
		AU-B- 556584	13-11-86
		AU-B- 8947382	03-05-84
		GB-A,B 2128500	02-05-84
		JP-C- 1866555	26-08-94
		JP-B- 3077819	11-12-91
		JP-A- 59081341	11-05-84
WO-A-9014054	29-11-90	US-A- 5152782	06-10-92
		DE-D- 69024212	25-01-96
		EP-A- 0473694	11-03-92
		JP-T- 4505720	08-10-92
US-A-4729914	08-03-88	DE-A- 3708954	06-10-88
		FR-A- 2612120	16-09-88
		GB-A- 2202762	05-10-88
		JP-A- 63238170	04-10-88
EP-A-0335308	04-10-89	DE-D- 68911181	20-01-94
		DE-T- 68911181	07-04-94
		JP-A- 1310665	14-12-89
		US-A- 5169720	08-12-92
WO-A-8911500	30-11-89	NONE	
US-A-4119094	10-10-78	US-A- 4100309	11-07-78
		AR-A- 219763	15-09-80
		AU-B- 512679	23-10-80
		AU-B- 3856878	05-06-80
		BE-A- 869588	01-12-78
		CA-A- 1109344	22-09-81
		CH-A- 639675	30-11-83
		CH-A- 634590	15-02-83
		DE-A- 2828617	01-03-79
		FR-A,B 2399879	09-03-79

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/GB 96/00725

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US-A-4119094		GB-A- 1600963	21-10-81
		JP-C- 1246290	25-12-84
		JP-A- 54029343	05-03-79
		JP-B- 59019582	07-05-84
		NL-A- 7808290	12-02-79
		SE-B- 441064	09-09-85
		SE-A- 7808442	10-02-79
EP-A-0443993	28-08-91	IT-B- 1240111	27-11-93
		DE-D- 69101458	28-04-94
		DE-T- 69101458	14-07-94
		ES-T- 2050521	16-05-94
		US-A- 5163954	17-11-92